

REMARKS

Status of the Claims

Claims 1-39 were pending.

Claims 17, 25, 28 and 32-39 were withdrawn from consideration in view of a restriction requirement.

Claims 1-16, 18-24, 26, 27, 30 and 31 stand rejected.

Claim 29 stands objected to.

Claims 17, 25, 28, 31, 33, and 39 are canceled herein.

Claims 1, 10, 14, 15, 18, 19, 20, 21, 22, 23, 26, 29, 32, 34, 35, 36, and 37 are amended herein.

Claims 40 and 41 are new claims.

Reconsideration is respectfully requested.

Response to Office Action

Applicant gratefully acknowledges that the Examiner found the subject matter of claim 29 to be allowable, if rewritten in independent form. Applicant has amended claim 29 to omit reference to the benzo-thiadiazine-1,1-dioxide species, which were the subject of the restriction requirement. It is believed that, with the amendments to claim 1 herein (discussed below), claim 29 is now allowable.

Applicant further gratefully acknowledges that no rejections have been asserted under Sections 102 and 103. It is believed all rejections under Section 112 have been addressed by the current amendments, discussed below.

With regard to the restriction requirement, applicant has canceled claims 17, 25, 28, 33, and 39, and the subject matter of claim 33 was incorporated into claim 32. Thus, Applicant has canceled the claims to compounds wherein Z is $-S(O)_2-$, and to the process of making compounds of Formula I, for the purpose of expediting the prosecution. Without waiver of the traversal previously set forth and that set forth below, Applicant elects for prosecution the invention of Group Ia. Applicant reserves the right to file a divisional application to the canceled subject matter.

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With regard to the subject matter of claims 32 through 37, applicant traverses the restriction requirement and requests reconsideration thereof. It is noted that MPEP § 806.05(h) provides that a product and process (or method) of using the product may be considered distinct inventions if (a) the process can be performed with a materially different product, or (b) the product as claimed can be used in a materially different process. Here, the method of treatment claims 32 through 37 are dependent upon the product claims, and thus, a *materially* different product is not included in the claimed method. With regard to paragraph (b), “the burden is on the examiner to provide an example” of a materially different method in which the claimed compounds may be used. Pursuant to this requirement, applicant respectfully submits that an example be provided or the restriction requirement be withdrawn.

Below is a discussion of the amendments to the specification and claims herein and new claims 40 and 41.

Amendments to the Specification

Applicant has amended the specification to address certain typographical errors and to amend the Summary of Invention to conform with the scope of claim 1 as amended herein, and to recite more specifically the valency of the bond between atoms X and Y, as suggested in the Office Action at page 3, ¶ 1. The amendments to the Summary of Invention are discussed below, with reference to claim 1.

Besides the Summary, at page 10, line 11, through page 11, line 16, certain typographical errors in the “Preferred compound” section are corrected. These corrections are a matter of form only, and do not present new matter.

At page 11, line 25, the definition of “alkyl” is corrected. It is noted that in the original specification, the identical definition was given for alkyl and lower alkyl, i.e., an alkyl of one to six carbon atoms. Additionally, in the definitions for both alkyl and lower alkyl, examples of lower alkyl are recited as including hexyl groups. Thus, one skilled in the field reading the original description would understand that a lower alkyl is alkyl of one to six carbon atoms, and an alkyl is an alkyl having greater than six carbon atoms, i.e., eight carbon atoms.

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The definition of substituted alkyl at page 12, line 3, was amended to correct a typographical error in the word hydroxy.

Accordingly, the amendments to the specification do not present new matter.

Amendments to the Claims

Claim 1 was amended to more specifically recite the valency of the bond between atoms X and Y, as suggested in the Office Action. With this amendment, it is believed the Section 112 rejection of claim 1 has been addressed.

Claim 1 was further amended in several respects for the purposes of clarity. For example, in a number of instances the substituents are recited as "one or more" substituents. This term was amended to recite "one, two or three" substituents, to avoid use of an open-ended term in the claim.

Claim 1 was amended to recite "haloalkyl" as an optional substituent on the ring formed by R^2 and R^3 , to provide antecedent basis for this term in claim 10. Applicant gratefully acknowledges the observation by the Examiner that "haloalkyl" in claim 10, lacks antecedent basis in claim 1. It is believed the basis for the Section 112 rejection of claim 10 has been removed.

Claim 1 was further amended to include within the scope thereof compounds wherein R^2 , R^3 , and R^4 are selected (individually, or R^2 and R^3 together), from a heterocyclyl in turn substituted with a phenyl, in turn having an optional substituent selected from lower alkoxy and closely-related groups. This amendment is made to encompass within the scope of claim 1 the compound **204**, recited at page 56, lines 5-6 of the specification, which has a piperidinyl group for R^2 , R^3 , or R^4 , in turn substituted with a phenyl group, in turn substituted with a methoxy.

Additionally, claim 1 was amended to recite compounds wherein R^2 , R^3 , and R^4 may be $-N=R''$, wherein R'' may be selected from heterocyclyl (more particularly recited in claim 40 as pyrrolidinyl and piperidinyl), in turn optionally substituted with one to two of hydroxy, oxo, cyano, cyanoalkyl, lower alkyl, and lower alkoxy. This amendment was made to encompass within the scope of claim 1 compounds **811** and **812** recited at page 70, lines 11-14 of the specification.

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Claim 10 was amended to delete the redundant reference to lower alkoxy, which was pointed out in the Office Action, and which applicant gratefully acknowledges.

Claims 14, 15, 18, 22 and 26 were amended to insert the missing preposition "to", or "to which," and to omit the word also, for sake of clarity.

Claims 29 and 32 have been amended as previously described, in response to the restriction requirement.

Claims 34 through 38 have been amended to depend upon claim 32, as opposed to claim 33, as claim 33 was canceled.

Claims 40 and 41 were added to more particularly recite the inventive compounds, in view of the examples. These two claims recite a more narrow subgenus to claim 1 compounds, providing more narrow coverage for the compounds exemplified in the specification. The selections recited in Claim 40 are supported by the particular examples set forth in the specification.

FEES

No fees should be due. Although two new claims are added, more than two claims have been canceled.

CONCLUSION

Applicant respectfully submits that all claims are now in condition for allowance, and that the instant application proceed to issuance. The Examiner is invited to contact the undersigned if it is believed a telephonic communication would expedite allowance of the instant application.

Respectfully submitted,



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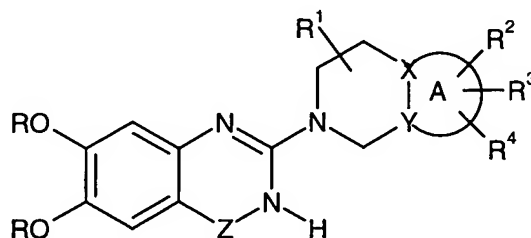
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APPENDIX A
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1 (Amended). A compound comprising Formula I:



wherein:

X is carbon or nitrogen;

Y is carbon;

and X-Y considered together are two adjoining atoms of the ring A, said ring being a fused aromatic ring of five to six atoms per ring optionally incorporating one to two heteroatoms per ring, chosen from N, O, or S ; wherein, when X is nitrogen, the bond between atoms X and Y is a single bond, and when X is carbon, the bond between atoms X and Y is double bond;

Z is -C(O)-;

each R is independently selected from lower alkyl;

R¹ is selected from:

hydrogen; lower alkyl;

aryl; arylalkyl; arylaminocarbonyl; wherein the aryl group is optionally substituted with one to two substituents selected from lower alkyl, halo, cyano and lower alkoxy; and

heteroaryl or heteroarylalkyl, wherein the aryl group is optionally substituted with one or two substituents selected from the group consisting of lower alkyl, halogen, cyano, and lower alkyl;

R², R³, and R⁴ are each independently in each occurrence selected from:

hydrogen; lower alkyl;

cycloalkyl or cycloalkylalkyl, wherein the cycloalkyl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halo-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, and phenyl optionally substituted with one or two substituents selected from the group consisting of lower alkyl, halogen, cyano and lower alkoxy;

aryl or arylalkyl, wherein the aryl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, and arylcarbonylamino, or two adjacent atoms of the aryl ring can be substituted with a methylenedioxy or ethylenedioxy group to form a fused heterocyclyl ring;

heterocyclyl or heterocyclylalkyl, wherein the heterocyclyl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, hydroxyalkyl, oxo, cyano, cyanoalkyl, lower alkyl, lower alkoxy, alkoxyalkyl, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, and phenyl optionally substituted with one or

two substituents selected from the group consisting of lower alkyl, halogen, cyano and lower alkoxy;

heteroaryl or heteroarylalkyl, wherein the heteroaryl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, and arylcarbonylamino;

hydroxy; hydroxyalkyl; alkoxy; alkoxyalkyl;

halo; haloalkyl; cyano; cyanoalkyl; and

$-(CH_2)_{0-3}NR'R''$; $-C(=NH)-NR'R''$; $-N-C(=NR')-R''$; $-N=CR'-NR'R''$; -

$SO_2NR'R''$; $-NSO_2R'$; $-C(O)R'$; $-C(O)NR'R''$; $-NC(O)R'$; or $-N=R'''$;

with the proviso that if A is a benzene ring, at least one of R^2 , R^3 or R^4 is not hydrogen; or

R^2 and R^3 , if adjacent, taken together with the carbons to which they are attached may form a 5- to 7- membered aromatic, saturated or unsaturated ring, optionally incorporating one or two ring heteroatoms chosen from N, S, or O, which can be optionally substituted with one or two substituents selected from lower alkyl, halo, haloalkyl, cyano, alkylthio, and lower alkoxy; and

R' and R'' are independently in each occurrence selected from:

hydrogen; lower alkyl; substituted lower alkyl;

hydroxyalkyl; alkoxyalkyl;

cycloalkyl, wherein the cycloalkyl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl,

arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, and phenyl;

aryl or arylalkyl, wherein the aryl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, and arylcarbonylamino, or two adjacent atoms of the aryl ring can be substituted with a methylenedioxy or ethylenedioxy group to form a fused heterocyclic ring;

heteroaryl or heteroarylalkyl, wherein the heteroaryl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, cyano, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, and arylcarbonylamino;

heterocyclyl or heterocyclylalkyl, wherein the heterocyclyl group is optionally substituted with one, two, or three substituents selected from the group consisting of hydroxy, oxo, cyano, cyanoalkyl, lower alkyl, lower alkoxy, halogen-lower alkoxy, alkylthio, halogen, haloalkyl, hydroxyalkyl, nitro, alkoxycarbonyl, amino, alkylamino, alkylsulfonyl, arylsulfonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonylamino, arylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino;

or R' and R" together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O or S; wherein this ring is optionally substituted with one or two substituents selected from the group consisting of lower alkyl, halogen, cyano, lower alkoxy and phenyl optionally substituted with one or two substituents selected from the group consisting of lower alkyl, halogen, cyano and lower alkoxy;

R''' is selected from heterocyclyl optionally substituted with one or two substituents selected from the group consisting of hydroxy, oxo, cyano, cyanoalkyl, lower alkyl, and lower alkoxy;

or individual isomers, racemic or non-racemic mixtures of isomers or pharmaceutically acceptable salts or solvates thereof.

2. (original) The compound of Claim 1, wherein X is carbon.
3. (original) The compound of Claim 1, wherein X is nitrogen.
4. (original) The compound of Claim 1, wherein R¹ is hydrogen.
5. (original) The compound of Claim 4, wherein X is carbon and A is a fused aryl ring.
6. (original) The compound of Claim 5, wherein A is a fused benzene ring.
7. (original) The compound of Claim 4, wherein X is carbon and A is a fused heteroaryl ring.
8. (original) The compound of Claim 7, wherein A is a fused pyrimidine ring.
9. (original) The compound of Claim 7, wherein A is a fused pyrrole ring.

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10. (amended) The compound of Claim 9, wherein R^2 and R^3 taken together with the carbons to which they are attached form a fused benzene ring, optionally substituted with one or two substituents selected from lower alkyl, halo, haloalkyl, cyano, alkylthio, or lower alkoxy.
11. (original) The compound of Claim 7, wherein A is a fused pyridine ring.
12. (original) The compound of Claim 7, wherein A is a fused imidazole ring.
13. (original) The compound of Claim 4, wherein X is nitrogen and A is a fused imidazole ring.
14. (amended) The compound of Claim 4, wherein R^2 is $-(CH_2)_{0-3}NR'R''$ or $-SO_2NR'R''$, and wherein R' and R'' are independently in each occurrence selected from hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R' and R'' together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O, or S.
15. (amended) The compound of Claim 6, wherein R^2 is $-(CH_2)_{0-3}NR'R''$ or $-SO_2NR'R''$, and wherein R' and R'' are independently in each occurrence selected from hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R' and R'' together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O, or S.
16. (original) The compound of Claim 15, wherein Z is $-C(O)-$.
17. (Canceled).

18. (amended) The compound of Claim 6, wherein R^2 is selected from the groups -C(NH)-NR'R", -N-C(NR')-R", and -N=CR'-NR'R", and wherein R' and R" are independently in each occurrence selected from hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R' and R" together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O, or S.
19. (amended) The compound of Claim 18, wherein Z is -C(O)-.
20. (amended) A compound of Claim 6, wherein R^2 is aryl or heteroaryl.
21. (amended) A compound of Claim 6, wherein R^2 is alkoxy, cyano, or cyanoalkyl.
22. (amended) The compound of Claim 8, wherein R^2 is -(CH₂)₀₋₃NR'R" or -SO₂NR'R", and wherein R' and R" are independently in each occurrence selected from hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R' and R" together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O, or S.
23. (amended) The compound of Claim 22, wherein R^2 is -NR'R", and wherein R' and R" are selected from hydrogen or alkyl, or R' and R" taken together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O, or S.
24. (original) The compound of Claim 22, wherein Z is -C(O)-.
25. (canceled).

- 26 (amended) The compound of Claim 13, wherein R^2 is $-(CH_2)_{0-3}NR'R''$ or $-SO_2NR'R''$, and wherein R' and R'' are independently in each occurrence selected from hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R' and R'' together with the nitrogen to which they are attached may form a 5- to 7- membered ring, optionally incorporating one additional ring heteroatom chosen from N, O or S.
27. The compound of Claim 26, wherein Z is $-C(O)-$.
- 28 (Canceled).
29. (Amended) The compound of Claim 1, wherein the compound is:
6,7-dimethoxy-2-[5-(4-methoxy-phenyl)-3,4-dihydro-1*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-[7-(4-methoxy-phenyl)-3,4-dihydro-1*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(4-morpholin-4-yl-5,8-dihydro-6*H*-pyrido[3,4-*d*]pyrimidin-7-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(5-pyridin-3-yl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
2-(4-benzylamino-5,8-dihydro-6*H*-pyrido[3,4-*d*]pyrimidin-7-yl)-6,7-dimethoxy-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(5-pyrrolidin-1-yl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(5-pyridin-4-yl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(5-pyrimidin-5-yl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
2-(6,7-dimethoxy-4-oxo-1,4-dihydro-quinazolin-2-yl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonic acid (2-pyridin-2-yl-ethyl)-amide;

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2-(6,7-dimethoxy-4-oxo-3,4-dihydro-quinazolin-2-yl)-6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline-5-carbonitrile;
6,7-dimethoxy-2-[5-(1*H*-pyrrol-2-yl)-3,4-dihydro-1*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one;
2-[5-(1*H*-imidazol-2-yl)-3,4-dihydro-1*H*-isoquinolin-2-yl]-6,7-dimethoxy-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-[4-(4-methyl-piperazin-1-yl)-5,8-dihydro-6*H*-pyrido[3,4-*d*]pyrimidin-7-yl]-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-{4-[(2-methoxy-ethyl)-methyl-amino]-5,8-dihydro-6*H*-pyrido[3,4-*d*]pyrimidin-7-yl}-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-[5-(morpholine-4-sulfonyl)-3,4-dihydro-1*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(4-piperidin-1-yl-5,8-dihydro-6*H*-pyrido[3,4-*d*]pyrimidin-7-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-[5-(1-morpholin-4-yl-methanoyl)-3,4-dihydro-3*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(1-phenyl-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl)-3*H*-quinazolin-4-one;
2-[1-(4-chloro-phenyl)-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl]-6,7-dimethoxy-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(1-naphthalen-2-yl-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-[1-(4-methoxy-phenyl)-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl]-3*H*-quinazolin-4-one;
2-[1-(3-chloro-phenyl)-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl]-6,7-dimethoxy-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(1-*m*-tolyl-1,4,6,7-tetrahydro-imidazo[4,5-*c*]pyridin-5-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(3-phenyl-5,6-dihydro-8*H*-imidazo[1,5-*a*]pyrazin-7-yl)-1*H*-quinazolin-4-one;

2-(3-cyclohexyl-5,6-dihydro-8*H*-imidazo[1,5-*a*]pyrazin-7-yl)-6,7-dimethoxy-1*H*-quinazolin-4-one;
6,7-dimethoxy-2-(1,3,4,9-tetrahydro- β -carbolin-2-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(6-methoxy-1,3,4,9-tetrahydro- β -carbolin-2-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(7-methylsulfanyl-1,3,4,9-tetrahydro- β -carbolin-2-yl)-3*H*-quinazolin-4-one;
2-(3,4-dihydro-1*H*-2,7,10-triaza-anthracen-2-yl)-6,7-dimethoxy-3*H*-quinazolin-4-one;
N-[2-(6,7-dimethoxy-4-oxo-3,4-dihydro-quinazolin-2-yl)-1,2,3,4-tetrahydro-isoquinolin-5-yl]-cyclopentanecarboxamidine;
6,7-dimethoxy-2-(5-morpholin-4-ylmethyl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
6,7-dimethoxy-2-(5-piperidin-1-ylmethyl-3,4-dihydro-1*H*-isoquinolin-2-yl)-3*H*-quinazolin-4-one;
2-[5-(4,5-dihydro-1*H*-imidazol-2-ylamino)-3,4-dihydro-1*H*-isoquinolin-2-yl]-6,7-dimethoxy-3*H*-quinazolin-4-one;
N-[2-(6,7-dimethoxy-4-oxo-3,4-dihydro-quinazolin-2-yl)-1,2,3,4-tetrahydro-isoquinolin-5-yl]-cyclobutanecarboxamidine;
N-[2-(6,7-dimethoxy-4-oxo-3,4-dihydro-quinazolin-2-yl)-1,2,3,4-tetrahydro-isoquinolin-5-yl]-butyramidine;
N-[2-(6,7-dimethoxy-4-oxo-3,4-dihydro-quinazolin-2-yl)-1,2,3,4-tetrahydro-isoquinolin-5-yl]-*N,N*-dimethyl-formamidine;
6,7-dimethoxy-2-[5-(1-methyl-4,5-dihydro-3*H*-pyrrol-2-ylamino)-3,4-dihydro-1*H*-isoquinolin-2-yl]-3*H*-quinazolin-4-one; or
2-[5-(4,5-dihydro-3*H*-pyrrol-2-ylamino)-3,4-dihydro-1*H*-isoquinolin-2-yl]-6,7-dimethoxy-3*H*-quinazolin-4-one; or a pharmaceutically-acceptable salt thereof.

30 (original).A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of Claim 1 in admixture with at least one pharmaceutically acceptable carrier.

31 (Canceled)

32. (Amended) A method of treating a subject having a disease state that is alleviated by treatment with an alpha-1A/B adrenoceptor antagonist, which method comprises administering to the subject a therapeutically effective amount of at least one compound of Claim 1.

33 (Canceled)

34 (Amended) The method of Claim 32 wherein the disease state comprises disorders and symptoms of the urinary tract.

35 (Amended) The method of Claim 32 wherein the disease state comprises improvement of sexual dysfunction.

36 (Amended) The method of Claim 32 wherein the disease state comprises benign prostatic hypertrophy and the irritative symptoms associated with ~~#~~ benign prostatic hypertrophy.

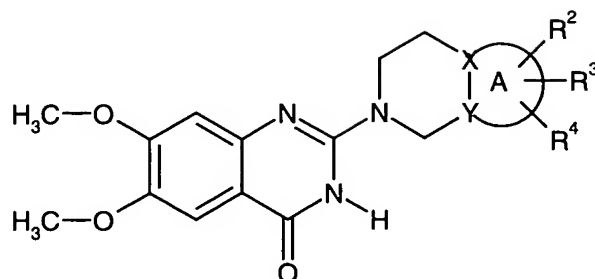
37 (Amended) The method of Claim 32 wherein the disease state comprises pain.

38 (original) The method of Claim 37 wherein the disease state comprises inflammatory pain, neuropathic pain, cancer pain, acute pain, chronic pain, or complex regional pain syndromes.

40 (Canceled)

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40 (New). A compound having the formula,



wherein:

X is carbon or nitrogen;

Y is carbon; and X-Y considered together are two adjoining atoms of the ring A, said ring being selected from a fused benzo, pyrrolyl, imidazolyl, pyridyl, or pyrimidinyl ring; wherein when X is nitrogen, the bond between atoms X and Y is a single bond, and when X is carbon, the bond between atoms X and Y is double bond; and

R², R³, and R⁴ are each independently in each occurrence selected from:

hydrogen; lower alkyl;

hydroxy; hydroxyalkyl; alkoxy; alkoxyalkyl;

halo; haloalkyl; cyano; cyanoalkyl;

cyclopentyl, cyclohexyl, or cycloheptyl;

phenyl, phenyl(lower alkyl), pyridyl, pyridyl(lower alkyl) pyrimidinyl,

pyrimidinyl(lower alkyl), pyrazinyl, pyrazinyl (lower alkyl), pyrrolyl,

pyrrolyl(lower alkyl), imidazolyl, imidazolyl(lower alkyl), and naphthyl,

each of said aryl and heteroaryl rings in turn optionally substituted with one to two halogen, lower alkoxy, lower alkyl, trifluoromethyl, methylthiol, and/or amino;

morpholinyl, morpholinyl(lower alkyl), piperidinyl, piperidinyl(lower alkyl),

piperazinyl, piperazinyl(lower alkyl) pyrrolidinyl, pyrrolidinyl(lower alkyl), imidazolidinyl, imidazolidinyl(lower alkyl), tetrahydrofuryl,

tetrahydrofuryl(lower alkyl), and 1-H-pyrimidine-2,4-dione, each of said heterocyclic rings in turn optionally substituted with one to two of hydroxy, oxo, lower alkoxy, hydroxy(lower alkyl), and/or phenyl, said phenyl in turn optionally substituted with one or two substituents selected from the group consisting of lower alkyl, halogen, cyano and lower alkoxy;

$-(CH_2)_{0-3}NR'R''$; $-SO_2NR'R''$; $-C(O)R'$; $-C(=NH)-NR'R''$; $-N-C(=NH)-R''$; $-N=CR'-NR'R''$; and $-N=R'''$;

or R^2 and R^3 taken together form a fused pyridyl or a methylenedioxy or ethylenedioxy group to form a fused heterocyclic ring;

with the proviso that if A is a benzene ring, at least one of R^2 , R^3 or R^4 is not hydrogen;

R and R'' are individually selected from hydrogen, lower alkyl, lower alkoxy, hydroxyalkyl, phenyl, phenyl(lower alkyl), pyridyl, pyridyl(lower alkyl), pyrrolidinyl, furyl, imidazolidinyl, piperidinyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, morpholinyl, said rings in turn optionally substituted with lower alkyl, lower alkoxy, cyano(lower alkyl), 5,6-dihydro-2H-thiazin-3-yl;

or alternatively, R' and R'' together with the nitrogen to which they are attached may form a piperidinyl or morpholinyl ring optionally substituted with one or two substituents selected from the group consisting of lower alkyl, lower alkoxy, cyano, or cyano(lower alkyl); and

R''' is selected from pyrrolidinyl and piperidinyl in turn optionally substituted with up to one lower alkyl, lower alkoxy, cyano, or cyano(lower alkyl).

42 (New). A compound according to claim 41, in which X is carbon and A is a fused aryl, pyridyl, or pyrimidinyl ring.